VIA ELECTRONIC FILING

APPELLANTS' BRIEF	Application Number	10/748,897
	Confirmation Number	7432
	Attorney Docket No.	PALO-002
	Filing Date	December 29, 2003
	First Named Inventor	Anthony Joonkyoo Yun
Address to: Mail Stop Appeal Brief-Patents Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Examiner	Umamaheswari Ramachandran
	Group Art	1617
	Title: "Treatment of Conditions Through Pharmacological Modulation of the Autonomic Nervous System"	

Sir:

This Brief is filed in support of Appellants' appeal from the Examiner's Rejection dated November 29, 2007, and the Advisory Action dated February 22, 2008. No claims have been allowed. Claims 1, 3, 4, 11-28, 41, 62 and 63 are pending and are appealed herein. A Notice of Appeal was filed on April 29, 2008.

The Board of Appeals and Interferences has jurisdiction over this appeal pursuant to 35 U.S.C. §134.

Provided herewith is an authorization to charge deposit account number to Deposit Account No. 50-0815, order number PALO-002, to cover the fee required under 37 C.F.R. §41.20(b)(2) for filing Appellants' Brief. In the unlikely event that the fee transmittal or other papers are separated from this document and/or other fees or relief are required, Appellants petition for such relief, including extensions of time, and authorize the Commissioner to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to deposit Account No. 50-0815, order number PALO-002.

TABLE OF CONTENTS

CONTENTS	PAGE
Real Party in Interest	3
Related Appeals and Interferences	3
Status of Claims	3
Status of Amendments	3
Summary of Claimed Subject Matter	3
Grounds of Rejection to be Reviewed on Appeal	6
Argument	7
Summary	26
Relief Requested	28
Claims Appendix	29
Evidence Appendix	33
Related Proceedings Appendix	34

REAL PARTY IN INTEREST

The inventors named on this patent application assigned their entire rights to the invention to Palo Alto Investors.

RELATED APPEALS AND INTERFERENCES

There are currently no other appeals or interferences known to Appellants, the undersigned Appellants' representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.

STATUS OF CLAIMS

The present application was filed on December 29, 2003 with Claims 1-61. During the course of prosecution, Claims 62 and 63 were added, Claims 29-40 and 42-61 were withdrawn, and Claims 2 and 5-10 were canceled. Accordingly, Claims 1, 3, 4, 11-28, 41, 62 and 63 are pending and under examination in the present application, all of which are appealed herein.

STATUS OF AMENDMENTS

No amendments to the Claims were filed subsequent to issuance of the Final Rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is drawn to methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

Independent Claim 1 claims a method of treating a subject for a condition caused by an autonomic nervous system abnormality comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for at least one of:

neurodegenerative conditions; neuroinflammatory conditions; orthopedic inflammatory conditions; lymphoproliferative conditions; autoimmune conditions; inflammatory conditions; infectious diseases, pulmonary conditions; transplant-related conditions, gastrointestinal conditions; endocrine conditions; genitourinary conditions selected from the group of renal failure, hyperreninemia, hepatorenal syndrome and pulmonary renal syndrome; aging associated conditions; neurologic conditions; Th-2 dominant conditions; conditions that cause hypoxia; conditions that cause hypercarbia; conditions that cause hypercapnia; conditions that cause acidosis; conditions that cause acidemia, pediatric-related conditions; OB-GYN conditions, sudden death syndromes, fibrosis; post-operative recovery conditions; post-procedural recovery conditions; chronic pain; disorders of thermoregulation, cyclic vomiting syndrome and trauma, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system (see specification for example on p. 2, lines 1-5; p. 9, lines 3-12; p. 10, lines 11-15; and p. 57, line 10 to p. 59, line 10)).

Claim 3 is dependent on Claim 1 and specifies that the abnormality is characterized by a sympathetic bias (see the specification for example on p. 10, lines 15-19; and p. 12, lines 14-18). Claim 4 is dependent on Claim 1 and specifies that the abnormality is characterized by a parasympathetic bias (see the specification for example on p. 12, lines 8-13).

Claim 11 is dependent on Claim 1 and specifies that the abnormality is characterized by an abnormally high parasympathetic activity (see the specification for example on p. 11, lines 20-27; and p. 56, lines 29-31). Claim 12 is dependent on Claim 11 and further specifies that the abnormality is characterized by an abnormally low sympathetic activity (see the specification for example on p. 11, lines 20-27; and p. 56, lines 29-31). Claim 13 depends on Claim 11 and further specifies that the abnormality is characterized by normal sympathetic activity (see the specification for example on p. 11, lines 20-27; and p. 56, line 29 to p. 57, line 2). Claim 14 depends on Claim 11 and further specifies that the abnormality is characterized by an abnormally high sympathetic activity (see the specification for example on p. 13, lines 5-9; and p. 56, line 29 to p. 57, line 2). Claim 15 is dependent on Claim 11 and further specifies decreasing the abnormally high parasympathetic activity (see the specification for example on p. 12, lines 8-13).

Claim 16 is dependent on Claim 1 and specifies that the abnormality is characterized by an abnormally low parasympathetic activity (see the specification for example on p. 12, line 31 to p. 13, line 11). Claim 17 is dependent on Claim 16 and further specifies that the abnormality is characterized by an abnormally low sympathetic activity (see the specification for example on p. 56, line 29 to p. 57, line 2). Claim 18 is dependent on Claim 16 and further specifies that the abnormality is characterized by normal sympathetic activity (see the specification for example on p. 13, lines 9-11; p. 56 line 29 to p. 57, line 2). Claim 19 depends on Claim 16 and further specifies that the abnormality is characterized by an abnormally high sympathetic activity (see the specification for example on p. 13, lines 9-11; p. 56 line 29 to p. 57, line 2).

Claim 20 depends on Claim 4 and further specifies increasing parasympathetic activity (see the specification for example on p. 12, lines 8-13; and p. 52 lines 24-29). Claim 21 depends on Claim 1 and further specifies that at least one beta-blocker is chosen from atenolol, betaxolol, bisoprolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, pindolol, propranolol, sotalol, timolol, acebutalol, oxprenolol, carvedilol, and entbutolol (see the specification for example on p. 24, line 23 to p. 25 line 24). Claim 22 depends on Claim 1 and further specifies that the method comprises increasing the parasympathetic activity/sympathetic activity ratio in at least a portion of the subject's autonomic nervous system (see the specification for example on p. 52, lines 5-8 and lines 26-29; p. 53 lines 1-6).

Claim 23 depends on Claim 1 and further specifies administering an effective amount of at least one non-beta-blocker agent (see the specification for example on p. 21, lines 5-14; p. 25 line 5 to p. 26, line 9). Claim 24 depends on Claim 23 and further specifies that the at least one non-beta-blocker agent is chosen from aldosterone antagonists; angiotensin II receptor blockades; angiotensin converting enzyme inhibitors; statins; triglycerides lowering drugs; niacin; anti-diabetes agents; immunomodulators; nicotine; sympathomimetics; cholinergics; acetylcholinesterase inhibitors; magnesium and magnesium sulfates, calcium channel blockers; muscarinics; sodium channel blockers; glucocorticoid receptor blockers; peripheral andrenergic inhibitors; blood vessel dilators; central agonists; combined alpha and beta-blockers; alpha blockers; combination diuretics; potassium sparing diuretics; nitrates; cyclic nucleotide monophosphodiesterase inhibitors; alcohols; catecholamines inhibitors;

analgesics; neurotoxins; vasopressin inhibitors; oxytocin inhibitors; alcohol; relaxin hormone; renin inhibitors; estrogen; estrogen analogues; estrogen metabolites; progesterone inhibitors; testosterone inhibitors; gonadotropin-releasing hormone analogues; gonadotropin-releasing hormone inhibitors; vesicular monoamine transport inhibitors; dipeptidyl peptidase IV inhibitors; antihistamines and melatonin (see the specification for example on p. 27, line 6 to p. 30 line 21). Claim 25 depends on Claim 23 and further specifies that the at least one beta-blocker and the at least one non-beta-blocker are concomitantly administered in unit dosage form (see the specification for example on p. 23, line 26 to p. 24 line 10; and p. 25, line 26 to p. 26 line 9).

Claim 26 depends on Claim 1 and further specifies stimulating at least a portion of the subject's autonomic nervous system (see the specification for example on p. 51, lines 1-7). Claim 27 depends on Claim 26 and further specifies that stimulating comprises contacting at least a portion of said subject's autonomic nervous system with at least one electrode and applying electrical energy to at least a portion of said subject's autonomic nervous system (see the specification for example on p. 52, lines 21-31; p. 54, lines 13-21; p. 73, lines 19-28).

Claim 28 depends on Claim 1 and further specifies that the at least one beta-blocker is administered orally at least once a day to the subject (see the specification for example on p. 31, lines 23-26; p. 32, lines 1-3). Claim 41 depends on Claim 1 and further specifies that the condition is an aging associated condition chosen from the group of shy dragers, multi-system atrophy, age related inflammation conditions, and cancer (see the specification for example on p. 58, lines 14-16). Claim 62 depends on Claim 1 and further specifies that treating is for a period of at least 24 hours (see the specification for example on p. 15, lines 2-3). Claim 63 depends on Claim 1 and further specifies increasing parasympathetic activity (see the specification for example on p. 52, lines 24-29).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62 and 63 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Gambardella et al. (Metabolism, 46, 3, March 1999, p. 291-297).

II. Claims 1, 3, 4, 21, 28, and 41 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Brevetti et al. (Brief communications, Nov. 1981, p 938-941).

III. Claims 1 and 21 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Nordling et al. (E Urol, 1992, 21, 328-331).

IV. Claims 1, 3, 4, 11-12, 15, 17, 21 and 22 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4).

V. Claims 1, 21, 23-25, and 28 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Davies, et al. (The J of Intl Med Research, 1988, 16, 173-181).

VI. Claims 1 and 26-27 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Hill, et al. (U.S. Patent 6,449,507).

ARGUMENT

I. Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62 and 63 are patentable under 35 U.S.C. § 103(a) over Gambardella et al. (Metabolism, 46, 3, March 1999, p. 291-297).

In the arguments set forth below, the Appellants will argue the rejected claims in Groups as follows:

Group 1A: Claims 1, 3, 4, 13, 14, 16, 19-22, 28, 41, and 62
Group 1B: Claim 18
Group 1C: Claim 63

In the Final Office Action and the Advisory Action, the Examiner rejected Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62 and 63 as being unpatentable under 35 U.S.C. § 103(a) over Gambardella et al. (Metabolism, 46, 3, March 1999, p. 291-297).

In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must first demonstrate that the combined prior art references teach or suggest all the claimed limitations. In *Graham v. John Deere*, the Supreme Court set out a framework for applying the statutory language of 35 U.S.C. § 103. *Graham v. John Deere*, 383 US 1; 148 USPQ 459 (1966). This framework was reiterated in the Court's recent *KSR v. Teleflex Inc.* opinion, as follows:

> "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented."

KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1734 (2007).

The above framework may be restated as the following four factual inquires:

(A) Determining the scope and contents of the prior art;

(B) Ascertaining the differences between the prior art and the claims in issue;

(C) Resolving the level of ordinary skill in the pertinent art; and

(D) Evaluating evidence of secondary considerations.

With respect to framework elements A and B, courts have held that the reference or references cited in a rejection based on obviousness must teach or suggest all the elements of the claimed invention. "Subsumed within the Graham factors is a subsidiary requirement articulated by this court that where, as here, all claim limitations are found in a number of prior art references, the burden falls on the challenger of the patent to show by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so." Pfizer v. Apotex, 82 U.S.P.Q.2d 1321, 1330

(March 22, 2007). *See also Pharmastem Therapeutics v. Viacell et al.*, 83. U.S.P.Q. 2d 1289, 1302 (Fed. Cir. 2007) ("the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make [every element of] the composition or device, or carry out the [entire] claimed process, and would have had a reasonable expectation of success in doing so," (*citing KSR Int'l Co. v. Teleflex Inc.*, 82. U.S.P.Q.2d 1385 (2007); *and see Omegaflex, Inc. v. Parker-Hannifin Corp.*, 2007 U.S. App. LEXIS 14308 (Fed. Cir. 2007) ("[t]he Supreme Court recently explained that 'a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art,' (*citing KSR Int'l Co.* at 1741); *and see Dystar Textilfarben GmbH v. C.H. Patrick Co.*, 464 80 U.S.P.Q.2d 1641, 1646 (Fed. Cir. 2006) ("[once] all claim limitations are found in a number of prior art references, the factfinder must determine '[w]hat the prior art teaches, whether it teaches away from the claimed invention, and whether it motivates a combination of teachings from different references,' (*citing In re Fulton*, 391 F.3d 1195, 1199-1200 (Fed. Cir. 2004))).

The requirement that the combination of references teach or suggest all elements of the claimed invention has been endorsed by the Patent & Trademark Office. According to the post-KSR Patent Office promulgated examination guidelines on determination of obviousness, when office personnel reject claims by attempting to combine prior art elements according to allegedly known methods to yield predictable results, the Office must resolve the *Graham* factual inquiries and articulate:

(1) "a finding that the prior art included each element claimed, although not necessarily in a single prior art reference, with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a single prior art reference;"

(2) "a finding that one of ordinary skill in the art could have combined the elements as claimed by known methods, and that in combination, each element merely would have performed the same function as it did separately; and"

(3) "a finding that one of ordinary skill in the art would have recognized that the results of the combination were predictable." (Federal Register / Vol. 72, No. 195 / Wednesday, October 10, 2007 / Notices at 57529, *citing KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395 (US 2007)).

Thus, the rationale to support a conclusion that a claim would have been obvious is that "all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions," and that "the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention." *Id.* at 57529.

In *KSR*, the Court noted that any analysis supporting a rejection under § 103(a) must be made explicit, and that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements in the manner claimed." *KSR*, 127 S. Ct. at 1741. Put another way, the Court stated that it is important to "determine whether there was an apparent reason to combine the known elements in the way a patent claims." *Id.* "This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." *Id.*

It is respectfully submitted that the Examiner's *prima facie* case of obviousness is deficient because the cited prior art fails to teach or suggest each and every claim limitation found in the claims of the instant application. Below are the contentions of the Appellants with respect to the grounds of rejection as stated above, with a separate subheading for each group of claims presented.

Group 1A: Claims 1, 3, 4, 13, 14, 16, 19-22, 28, 41, and 62

The Claims of Group 1A specify methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

The Examiner has rejected the claims of this group as being obvious over Gambardella, and asserts that the cited reference teaches or suggests every element of the claims.

For the reasons detailed below, the Appellants submit that the cited reference

fails to make obvious the rejected claims. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of modulating the autonomic nervous system, such that said modulating results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system, as is claimed.

In rejecting the present claims, the Examiner has noted (Final Office Action of 11/29/2007, p. 8), "Gambardella et al. does not explicitly teach that modulating the autonomic nervous system results in substantially equal parasympathetic or sympathetic functions in at least a portion of said autonomic nervous system."

However, the Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time of the invention from Gambardella's teachings that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system in cancer patients and that substantially equal parasympathetic and sympathetic functions can be reached by modulating such activities. (Advisory Action, p. 2).

The Appellants respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggests all the claimed limitations. The Office has not pointed to where Gambardella discloses achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Gambardella fails to teach or suggest this element because the method in Gambardella discloses the use of propranolol in elderly weight-losing cancer patients to block the effects of the sympathetic nervous system. The goal of treatment disclosed in Gambardella is enhancement of daily caloric intake without increased energy expenditure (abstract). After administering propranolol, a decrease in energy expenditure is noted (Fig. 2), indicating a decrease in the basal metabolic rate (BMR) in these patients.

The Appellants maintain that it is entirely possible that in treating weight-losing patients with propranolol as in Gambardella, the desired treatment goal of a decrease in BMR could be achieved before reaching a situation where the sympathetic and parasympathetic activity is substantially equal. In other words, a patient could be successfully treated with propranolol, resulting in a measured decrease in energy

expenditure or BMR, without ever achieving a stage where the sympathetic and parasympathetic function is substantially equal.

The Appellants therefore maintain that Gambardella does not teach the element "wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system". Furthermore, Gambardella does not suggest this element, because the goal of treatment disclosed in Gambardella is enhancement of daily caloric intake without increased energy expenditure (abstract). There is no suggestion in Gambardella of a treatment goal wherein a stage is reached such that the sympathetic and parasympathetic function is substantially equal.

Accordingly, the Appellants contend that a *prima facie* case of obviousness has not been established, because Gambardella fails to teach or suggest treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Group 1B: Claim 18

Claim 18 of Group 1B specifies a method of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system, and wherein the abnormality comprises an abnormally low parasympathetic activity with normal sympathetic activity.

The Examiner has rejected the claim in this group as being obvious over Gambardella, and asserts that the cited reference teaches or suggests every element of the claim.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claim. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of using a beta-blocker to treat a condition characterized by normal sympathetic activity, as is claimed.

In rejecting Claim 18, the Examiner has stated that Gambardella "does not explicitly teach a method of treating conditions caused by abnormality in autonomic nervous system wherein the abnormality is characterized by normal sympathetic activity." (Office Action of 11/29/2007, p. 4). However, the Examiner alleges that it would have been obvious to administer a beta-blocker such as propranolol in treating a condition where the abnormality is characterized by normal sympathetic activity, and that the motivation to do so is provided by Gambardella because the reference teaches that propranolol is effective in the treatment of abnormality of the autonomic nervous system (Office Action of 11/29/2007, p. 4).

However, the Appellants respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. As discussed above, the Office agrees that Gambardella does not explicitly teach administering a beta-blocker such as propranolol in treating a condition where the abnormality is characterized by normal sympathetic activity. Gambardella does not teach this element because Gambardella discloses the use of propranolol in weight-losing cancer patients to block the effects of sympathetic bias. However, the Appellants maintain that Gambardella also does not suggest this element, because the patients in Gambardella all have a sympathetic bias. There is therefore no teaching or suggestion in Gambardella to use propranolol to treat patients with normal sympathetic activity as in current Claim 18.

Accordingly, the Appellants contend that a *prima facie* case of obviousness has not been established, because Gambardella fails to teach or suggest treating a condition with a beta-blocker wherein the abnormality comprises an abnormally low parasympathetic activity with normal sympathetic activity.

Group 1C: Claim 63

Claim 63 of Group 1C specifies a method of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic

functions in at least a portion of said autonomic nervous system, and wherein said method further comprises increasing parasympathetic activity.

The Examiner has rejected the claim in this group as being obvious over Gambardella, and asserts that the cited reference teaches or suggests every element of the claim.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claim. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of increasing parasympathetic activity, as is claimed.

In rejecting Claim 63, the Examiner alleges that in Gambardella, "by balancing the autonomic nervous system dysfunction in cancer patients by administration of propranolol the parasympathetic activity is increased" (Office Action of 11/29/2007, p. 3). The Examiner, however, does not point to where in Gambardella "increasing parasympathetic activity" is disclosed. The Appellants maintain that Gambardella does not teach increasing parasympathetic activity, because Gambardella is directed to the use of propranolol in elderly weight-losing cancer patients to block the effects of the sympathetic nervous system. Gambardella further does not suggest this element, because Gambardella only discloses a method of blocking the effects of the sympathetic nervous system. Nowhere in Gambardella is the element of increasing parasympathetic activity, as in current Claim 63.

Accordingly, a *prima facie* case of obviousness has not been established because Gambardella fails to teach or suggest all the elements of the rejected claims. Namely, Gambardella does teach or suggest treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system, and wherein said method further comprises increasing parasympathetic activity.

Therefore, in view of the discussion above, the Appellants submit that Gambardella et al. (Metabolism, 46, 3, March 1999, p. 291-297) fails to make obvious Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62 and 63 under 35 U.S.C. § 103(a) because Gambardella et al. fails to teach or suggest all the elements of the rejected claims. Consequently, the Appellants respectfully request that these rejections be withdrawn.

II. Claims 1, 3, 4, 21, 28, and 41 are patentable under 35 U.S.C. § 103(a) over Brevetti et al. (Brief communications, Nov. 1981, p 938-941).

In the arguments set forth below, the Appellants will argue the rejected claims in one group.

The claims of this group specify methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

The Examiner has rejected the claims of this group as being obvious over Brevetti, and asserts that the cited reference teaches or suggests every element of the claims.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claims. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of modulating the autonomic nervous system, such that said modulating results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system, as is claimed.

In rejecting the claims of this group, the Examiner has alleged that the reference teaches a sympathetic bias and a parasympathetic bias in at least a portion of the nervous system, and that in treating Shy-Drager syndrome a stage is reached where sympathetic and parasympathetic activities are substantially equal (Advisory Action, p. 2). The Appellants respectfully disagree.

In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. The Office has not pointed to where Brevetti discloses achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Brevetti discloses treatment of an imbalance between the alpha- and beta-adrenoreceptor activity of the sympathetic nervous system (p. 941), however there is no discussion of the parasympathetic nervous system. Nowhere does

Brevetti teach the element of modulating the autonomic nervous system which results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Furthermore, Brevetti does not suggest this element, because the reference teaches treatment for an imbalance in the sympathetic nervous system. As there is no discussion anywhere in Brevetti of the parasympathetic nervous system, there is no suggestion of the element of achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Therefore, a *prima facie* case of obviousness has not been established because Brevetti fails to teach or suggest all the elements of the rejected claims. Namely, Brevetti does not teach or suggest treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Consequently, the Appellants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1, 3, 4, 21, 28, and 41 be withdrawn.

III. Claims 1 and 21 are patentable under 35 U.S.C. § 103(a) over Nordling et al. (E Urol, 1992, 21, 328-331).

In the arguments set forth below, the Appellants will argue the rejected claims in one group.

The claims of this group specify methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of a subject's autonomic nervous system by administering an effective amount of at least one beta-blocker, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

The Examiner has rejected the claims of this group as being obvious over Nordling, and asserts that the cited reference teaches or suggests every element of the claims.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claims. Specifically, the Appellants submit that the

cited reference fails to teach or suggest the element of modulating the autonomic nervous system, such that said modulating results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system, as is claimed.

In rejecting the claims of this group, the Examiner alleges that it would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system by treating urethral inflammation, and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal (Final Office Action, p. 6).

The Appellants respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. The Office has not pointed to where Nordling discloses achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Nordling discloses the blockage of beta-adrenergic receptors of the sympathetic nervous system for the treatment of urethral inflammation, however nowhere in Nordling is there a specific discussion of the parasympathetic nervous system.

Furthermore, it is entirely possible that in treating urethral inflammation with propranolol as in Nordling, the desired treatment goal of a decrease in inflammation could be achieved before reaching a situation where the sympathetic and parasympathetic activity is substantially equal. In other words, treatment with propranolol could result in a decrease in inflammation, without ever achieving a stage where the sympathetic and parasympathetic function is substantially equal.

The Appellants therefore maintain that Nordling does not teach the element of a stage wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Furthermore, Nordling does not suggest this element, because the goal of treatment disclosed in Nordling is the treatment of urethral inflammation. There is no suggestion in Nordling of a treatment goal wherein a stage is reached such that the sympathetic and parasympathetic function is substantially equal.

Accordingly, the Appellants contend that a *prima facie* case of obviousness has

not been established, because Nordling fails to teach or suggest all the elements of the rejected claims. Namely, Nordling does not disclose treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Consequently, the Appellants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1 and 21 be withdrawn.

IV. Claims 1, 3, 4, 11-12, 15, 17, 21 and 22 are patentable under 35 U.S.C. § 103(a) over Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4).

In the arguments set forth below, the Appellants will argue the rejected claims in Groups as follows:

Group 2A: Claims 1, 3, 4, 11-12, 15, and 21
Group 2B: Claim 17
Group 2C: Claim 22

In the Final Office Action and the Advisory Action, the Examiner rejected Claims 1, 3, 4, 11-12, 15, 17, 21 and 22 as being unpatentable under 35 U.S.C. § 103(a) over Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4).

It is respectfully submitted that the Examiner's *prima facie* case of obviousness is deficient because the cited prior art fails to teach or suggest each and every claim limitation found in the claims of the instant application. Below are the contentions of the Appellants with respect to the grounds of rejection as stated above, with a separate subheading for each group of claims presented.

Group 2A: Claims 1, 3, 4, 11-12, 15 and 21

The Claims of Group 2A specify methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein

said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

The Examiner has rejected the claims of this group as being obvious over Majcherczyk, and asserts that the cited reference teaches or suggests every element of the claims.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claims. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of modulating the autonomic nervous system, such that said modulating results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system, as is claimed.

In rejecting the present claims, the Examiner has alleged that it would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system in the treatment of hypertension and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal (Final Office Action, p. 6).

The Appellants respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. The Office has not pointed to where Majcherczyk discloses achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Majcherczyk discloses that after treatment with beta-blockers, the activity in the renal sympathetic nerve is increased (p. 711), which argues against the hypothesis that the antihypertensive effect of beta-blockers is due to general sympathetic inhibition to all vascular areas (p. 713). The disclosure in Majcherczyk, therefore, is directed to the mechanism of action of beta-blockers in treating hypertension. Majcherczyk does not discuss effects on the parasympathetic nervous system, and nowhere in Majcherczyk is there the element of modulating of the autonomic nervous system which results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

The Appellants therefore maintain that Majcherczyk does not teach the element

of modulating of the autonomic nervous system which results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Furthermore, Majcherczyk does not suggest this element, because Majcherczyk is directed to the mechanism of action of beta-blockers in treating hypertension. There is no discussion in Majcherczyk of modulating the parasympathetic nervous system, and therefore there is no suggestion in Majcherczyk of reaching a stage such that substantially equal parasympathetic and sympathetic functions are achieved.

Therefore, the Appellants contend that a *prima facie* case of obviousness has not been established, because Majcherczyk fails to teach or suggest treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Group 2B: Claim 17

Claim 17 of Group 2B specifies a method of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system, and wherein the abnormality comprises an abnormally low parasympathetic activity with an abnormally low sympathetic activity.

The Examiner has rejected the claim in this group as being obvious over Majcherczyk, and asserts that the cited reference teaches or suggests every element of the claim.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claim. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of using a beta-blocker to treat a condition characterized by an abnormally low parasympathetic activity with an abnormally low sympathetic activity, as is claimed.

In rejecting Claim 17, the Examiner has alleged that Majcherczyk "inherently teaches....a low sympathetic activity" (Office Action, p. 6; Advisory Action, p. 2).

However, the Appellants respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. The Examiner has stated that the reference "inherently" teaches a low sympathetic activity, however the Examiner has not pointed to where Majcherczyk discloses treatment for a condition with an abnormally low sympathetic activity. Majcherczyk only discloses treatment of hypertensive rats. There is no disclosure in Majcherczyk of treating a condition with an abnormally low sympathetic activity.

The Appellants therefore maintain that Majcherczyk does not teach the element of treating a condition with an abnormally low sympathetic activity. Furthermore, Majcherczyk does not suggest this element, because Majcherczyk is directed to sympathetic responses to beta-blockers in treating hypertensive rats. There is no specific discussion in Majcherczyk of modulating the parasympathetic nervous system, and therefore there is no suggestion in Majcherczyk of modulating of the autonomic nervous system such that substantially equal parasympathetic and sympathetic functions are achieved.

Accordingly, the Appellants contend that a *prima facie* case of obviousness has not been established, because Majcherczyk fails to teach or suggest the element of using a beta-blocker to treat a condition characterized by an abnormally low parasympathetic activity with an abnormally low sympathetic activity.

Group 2C: Claim 22

Claim 22 of Group 2C specifies a method of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system, and wherein the method comprises increasing the parasympathetic/sympathetic activity ratio in at least a portion of the subject's autonomic nervous system.

The Examiner has rejected the claim in this group as being obvious over Majcherczyk, and asserts that the cited reference teaches or suggests every element of the claim.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claim. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of using a beta-blocker to treat a condition wherein the method comprises increasing the parasympathetic/sympathetic activity ratio in at least a portion of the subject's autonomic nervous system, as is claimed.

In rejecting Claim 22, the Examiner has not pointed to where Majcherczyk discloses the element of increasing the parasympathetic activity/ sympathetic activity ratio in at least a portion of the autonomic nervous system. As discusssed above, the Appellants maintain that Majcherczyk does not disclose this element because Majcherczyk does not specifically discuss parasympathetic activity. Additionally, nowhere in Majcherczyk is there a disclosure of a parasympathetic activity/ sympathetic activity ratio.

The Appellants therefore maintain that Majcherczyk does not teach the element of increasing the parasympathetic activity/ sympathetic activity ratio in at least a portion of the autonomic nervous system. Furthermore, Majcherczyk does not suggest this element, because Majcherczyk is directed to sympathetic responses to beta-blockers in treating hypertensive rats. There is no discussion in Majcherczyk of the parasympathetic nervous system, or of modulating the parasympathetic nervous system. There is therefore no suggestion in Majcherczyk of increasing the parasympathetic activity/ sympathetic activity ratio.

Accordingly, the Appellants contend that a *prima facie* case of obviousness has not been established, because Majcherczyk fails to teach or suggest all the elements of the rejected claims. Namely, Majcherczyk does not teach or suggest treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. In addition, Majcherczyk does not teach or suggest a method of treating a subject for a condition caused by an autonomic nervous system abnormality wherein the abnormality comprises an abnormally low parasympathetic activity with an

abnormally low sympathetic activity, as in Claim 17, nor does Majcherczyk disclose the element of increasing the parasympathetic activity/ sympathetic activity ratio in at least a portion of the autonomic nervous system, as in Claim 22.

Consequently, in view of the discussion above, the Appellants submit that Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4) fails to make obvious Claims 1, 3, 4, 11-12, 15, 17, 21 and 22 under 35 U.S.C. § 103(a) because Majcherczyk fails to teach or suggest all the elements of the rejected claims. Therefore, the Appellants respectfully request that these rejections be withdrawn.

V. Claims 1, 21, 23-25, and 28 are patentable under 35 U.S.C. § 103(a) over Davies, et al. (The J of Intl Med Research, 1988, 16, 173-181).

In the arguments set forth below, the Appellants will argue the rejected claims in one group.

The claims this group specify methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

The Examiner has rejected the claims of this group as being obvious over Davies, and asserts that the cited reference teaches or suggests every element of the claims.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claims. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of modulating the autonomic nervous system, such that said modulating results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system, as is claimed.

In rejecting the claims of this group, the Examiner has alleged that it would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic

activities of the autonomic nervous system in the treatment of hypertension and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal and that the reference teaches that parasympathetic nerves influence cerebral blood flow during hypertension (Final Office Action, p. 7).

The Appellants, however, respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. The Office has not pointed to where Davies teaches achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Davies discloses that ibuprofen does not substantially affect the treatment of hypertension in patients who are taking beta-blockers or thiazides, however there is no discussion in Davies of the autonomic nervous system. Nowhere in Davies is there disclosure of the element of modulating of the autonomic nervous system, and there is no disclosure of the element of achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Therefore, the Appellants maintain that Davies does not teach the element of achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Furthermore, Davies does not suggest this element, because the reference teaches that ibuprofen does not substantially affect the treatment of hypertension in patients who are taking beta-blockers or thiazides. As there is no discussion anywhere in Davies of the autonomic nervous system, there is no suggestion of the element of achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Therefore, a prima facie case of obviousness has not been established because Davies fails to teach or suggest all the elements of the rejected claims. Namely, Davies does not disclose treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Consequently, the Appellants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1, 21, 23-25, and 28 be withdrawn.

IV. Claims 1 and 26-27 are patentable under 35 U.S.C. § 103(a) over Hill, et al.

(U.S. Patent 6,449,507).

In the arguments set forth below, the Appellants will argue the rejected claims in one group.

The claims this group specify methods of treating a subject for a condition caused by an autonomic nervous system abnormality, comprising modulating at least a portion of the subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to the subject to treat the subject for the condition, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

The Examiner has rejected the claims of this group as being obvious over Hill, and asserts that the cited reference teaches or suggests every element of the claims.

For the reasons detailed below, the Appellants submit that the cited reference fails to make obvious the rejected claims. Specifically, the Appellants submit that the cited reference fails to teach or suggest the element of modulating the autonomic nervous system, such that said modulating results in substantially equal parasympathetic or sympathetic functions in at least a portion of the autonomic nervous system, as is claimed.

In rejecting the claims of this group, the Examiner has alleged that it would have been obvious to one of ordinary skill in the art at the time of the invention that administration of propranolol modulates or alters the sympathetic and parasympathetic activities of the autonomic nervous system, as Hill teaches the stimulation of parasympathetic and sympathetic nerve fibers and when balancing such activities a stage is reached where sympathetic and parasympathetic activities are substantially equal.

The Appellants respectfully disagree. In order to meet its burden in establishing a rejection under 35 U.S.C. § 103 the Office must demonstrate that the prior art reference teaches or suggest all the claimed limitations. Hill discloses a method for adjusting the beating of the heart to allow a medical procedure to be performed, in which the heart rate may be increased or decreased. There is no disclosure in Hill that teaches that the process of increasing or decreasing the heart rate during a medical procedure will result in substantially equal parasympathetic and sympathetic functions in

at least a portion of the autonomic nervous system. In other words, a patient could have a successful operation using the methods in Hill, without ever achieving a stage where the sympathetic and parasympathetic function is substantially equal.

Therefore, the Appellants maintain that Hill does not teach the element of achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Furthermore, Hill does not suggest this element, because the goal of treatment in Hill is to adjust the beating of the heart to allow a medical procedure to be performed. There is therefore no suggestion of the element of achieving substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system.

Therefore, a prima facie case of obviousness has not been established because Hill fails to teach or suggest all the elements of the rejected claims. Namely, Hill does not disclose treating a condition wherein modulating of the autonomic nervous system results in substantially equal parasympathetic and sympathetic functions in at least a portion of the autonomic nervous system. Consequently, the Appellants respectfully request that the 35 U.S.C. § 103(a) rejection of Claims 1 and 26-27 be withdrawn.

SUMMARY

I. Claims 1, 3, 4, 13, 14, 16, 18-22, 28, 41, 62 and 63 are not obvious under 35 U.S.C. § 103(a) over Gambardella et al. (Metabolism, 46, 3, March 1999, p. 291-297) because the reference fails to teach or suggest each and every element of this set of claims.

II. Claims 1, 3, 4, 21, 28, and 41 are not obvious under 35 U.S.C. § 103(a) over Brevetti et al. (Brief communications, Nov. 1981, p 938-941) because the reference fails to teach or suggest each and every element of this set of claims.

III. Claims 1 and 21 are not obvious under 35 U.S.C. § 103(a) over Nordling et al. (E Urol, 1992, 21, 328-331) because the reference fails to teach or suggest each and every element of this set of claims.

IV. Claims 1, 3, 4, 11-12, 15, 17, 21 and 22 are not obvious under 35 U.S.C. § 103(a) over Majcherczyk et al. (Br J Pharmacol, 1987, 91(4), 711-4) because the reference fails to teach or suggest each and every element of this set of claims.

V. Claims 1, 21, 23-25, and 28 are not obvious under 35 U.S.C. § 103(a) over Davies, et al. (The J of Intl Med Research, 1988, 16, 173-181) because the reference fails to teach or suggest each and every element of this set of claims.

VI. Claims 1 and 26-27 are not obvious under 35 U.S.C. § 103(a) over Hill, et al. (U.S. Patent 6,449,507 because the reference fails to teach or suggest each and every element of this set of claims.

RELIEF REQUESTED

The Appellants respectfully request that the rejections of Claims 1, 3, 4, 11-28, 41, 62 and 63 under 35 U.S.C. §103 (a) be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 12, 2008 By: /Lynn J. Kidder, Reg. No. 56,107/
Lynn J. Kidder
Registration No. 56,107

Date: June 12, 2008 By: /Bret Field, Reg. No. 37,620/
Bret Field
Registration No. 37,620

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\PALO\002\Palo 002 Appeal Brief.DOC

CLAIMS APPENDIX

1. A method of treating a subject for a condition caused by an autonomic nervous system abnormality comprising modulating at least a portion of said subject's autonomic nervous system by administering an effective amount of at least one beta-blocker to said subject to treat said subject for at least one of: neurodegenerative conditions; neuroinflammatory conditions; orthopedic inflammatory conditions; lymphoproliferative conditions; autoimmune conditions; inflammatory conditions; infectious diseases, pulmonary conditions; transplant-related conditions, gastrointestinal conditions; endocrine conditions; genitourinary conditions selected from the group of renal failure, hyperreninemia, hepatorenal syndrome and pulmonary renal syndrome; aging associated conditions; neurologic conditions; Th-2 dominant conditions; conditions that cause hypoxia; conditions that cause hypercarbia; conditions that cause hypercapnia; conditions that cause acidosis; conditions that cause acidemia, pediatric-related conditions; OB-GYN conditions, sudden death syndromes, fibrosis; post-operative recovery conditions; post-procedural recovery conditions; chronic pain; disorders of thermoregulation, cyclic vomiting syndrome and trauma, wherein said modulating results in substantially equal parasympathetic and sympathetic functions in at least a portion of said autonomic nervous system.

3. The method of Claim 1, wherein said abnormality is characterized by a sympathetic bias.

4. The method of Claim 1, wherein said abnormality is characterized by a parasympathetic bias.

11. The method of Claim 1, wherein said abnormality is characterized by an abnormally high parasympathetic activity.

12. The method of Claim 11, wherein said abnormality is characterized by an abnormally low sympathetic activity.

13. The method of Claim 11, wherein said abnormality is characterized by normal sympathetic activity.

14. The method of Claim 11, wherein said abnormality is characterized by an abnormally high sympathetic activity.

15. The method of Claim 11, further comprising decreasing said abnormally high parasympathetic activity.

16. The method of Claim 1, wherein said abnormality comprises an abnormally low parasympathetic activity.

17. The method of Claim 16, wherein said abnormality comprises an abnormally low sympathetic activity.

18. The method of Claim 16, wherein said abnormality comprises normal sympathetic activity.

19. The method of Claim 16, wherein said abnormality comprises an abnormally high sympathetic activity.

20. The method of Claim 4, further comprising increasing said parasympathetic activity.

21. The method of Claim 1, wherein said at least one beta-blocker is chosen from atenolol, betaxolol, bisoprolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, pindolol, propranolol, sotalol, timolol, acebutalol, oxprenolol, carvedilol, and entbutolol.

22. The method of Claim 1, wherein said method comprises increasing the parasympathetic activity/sympathetic activity ratio in at least a portion of said subject's autonomic nervous system.

23. The method of Claim 1, further comprising administering an effective amount of at least one non-beta-blocker agent.

24. The method of Claim 23, wherein said at least one non-beta-blocker agent is chosen from aldosterone antagonists; angiotensin II receptor blockades; angiotensin converting enzyme inhibitors; statins; triglycerides lowering drugs; niacin; anti-diabetes agents; immunomodulators; nicotine; sympathomimetics; cholinergics; acetylcholinesterase inhibitors; magnesium and magnesium sulfates, calcium channel blockers; muscarinics; sodium channel blockers; glucocorticoid receptor blockers; peripheral andrenergic inhibitors; blood vessel dilators; central agonists; combined alpha and beta-blockers; alpha blockers; combination diuretics; potassium sparing diuretics; nitrates; cyclic nucleotide monophosphodiesterase inhibitors; alcohols; catecholamines inhibitors; analgesics; neurotoxins; vasopressin inhibitors; oxytocin inhibitors; alcohol; relaxin hormone; renin inhibitors; estrogen; estrogen analogues; estrogen metabolites; progesterone inhibitors; testosterone inhibitors; gonadotropin-releasing hormone analogues; gonadotropin-releasing hormone inhibitors; vesicular monoamine transport inhibitors; dipeptidyl peptidase IV inhibitors; antihistamines and melatonin.

25. The method of Claim 23, wherein said at least one beta-blocker and at least one non-beta-blocker are concomitantly administered in unit dosage form.

26. The method of Claim 1, further comprising stimulating at least a portion of said subject's autonomic nervous system.

27. The method of Claim 26, wherein said stimulating comprises contacting at least a portion of said subject's autonomic nervous system with at least one electrode and applying electrical energy to at least a portion of said subject's autonomic nervous system.

28. The method of claim 1 wherein said at least one beta-blocker is administered orally at least once a day to said subject.

41. The method of Claim 1, wherein said condition is an aging associated condition chosen from the group of: shy dragers, multi-system atrophy, age related inflammation conditions, and cancer.

62. The method of Claim 1, wherein said treating is for a period of at least 24 hours.

63. The method of Claim 1, wherein said method further comprises increasing parasympathetic activity.

EVIDENCE APPENDIX

No evidence that qualifies under this heading has been submitted during the prosecution of this application, and as such it is left blank.

RELATED PROCEEDINGS APPENDIX

As stated in the *Related Appeals and Interferences* section above, there are no other appeals or interferences known to Appellants, the undersigned Appellants' representative, or the assignee to whom the inventors assigned their rights in the instant case, which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal. As such this section is left blank.